

REMARKS

Claims 25-27 are under consideration. Reconsideration is requested.

Rejection under 35 USC § 112, first paragraph

Claims 25-27 stand rejected under 35 USC § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable a skilled artisan to make and use the invention. It remains the Examiner's view that physiological art is unpredictable, and that the disclosure in the specification is insufficient to support the breadth of the claims. This rejection is traversed for the following reasons.

The Examiner states that the claims encompass inducing the formation of an organ in vitro for any vertebrate species at any developmental stage of the embryo. It is his position, that since the term "stage" is not defined in the specification, that it refers to the developmental stage of xenopus, and that the scope of the claims is therefore limited to transplanting in vitro induced organ into the fetus of a vertebrate. Applicants respectfully disagree. The term "stage", as used herein, has a plain English language meaning, "a period or step in a progress, activity or development; *esp*: one of the distinguishable periods of growth and development of a plant or animal". (Merriam Webster's Collegiate Dictionary, tenth edition, Springfield Mass., 1993), and is not limited to the embryonic state, but can be applied to any distinguishable stage of embryonic, juvenile or adult stage, as will be appreciated by persons of skill in the art.

The Examiner also takes the position that insufficient stage marker gene DNAs are known, and that undue experimentation would be required to determine developmental stage-specific genomic markers without first carrying out undue experimentation to determine the developmental stage-specific genomic DNA markers for representative species of the broadly claimed genus. Applicants have provided ample evidence that myriad gene markers are available for human, rat and mouse. Similar techniques can be used to obtain such markers for any stage that may be of interest in other vertebrates. Furthermore, applicants have submitted a Declaration by Professor Makoto Asashima, a person skilled in the art, evincing the availability of such markers and the ability to practice this aspect of the invention without undue experimentation. In

the 117th JAMS Symposium, "Stem Cell and Cell Therapy-[I] Stem Cell Biology, 3, "To which extent organ formation is possible with undifferentiated cells". P.27, the present inventor, Professor Makoto Asashima, has stated, "Pronephric tubule is formed by treating undifferentiated cells (animal cap cells) of *Xenopus* embryo with activin and retinoic acid, and a timecourse analysis of genes after the treatment reveals that the genes express regularly just like a normal embryo. It is shown that the genes found by this method not only express in embryos of frogs and newts, but also involved in the formation of kidney in the early development of mammals such as mouse and human." This is also described in Development 128, 3105-3115, 2001, and Molecular and Cellular Biology 23, 1, 62-69, 2003.

Additionally, it is noted that step i) of claim 25 recites "**and/or by observation of organ tissues**", a process that does not require knowledge of genomic DNA markers, but that can be carried out using traditional anatomical, histological and other observation techniques familiar to those of skill in the art.

The Examiner then states that the term "blastula" refers to an early non-mammalian embryo, and that accordingly the invention is limited to a non-mammal. Applicants respectfully disagree. The invention has been clearly described to include mammals, as indicated by the paragraph spanning pages 6-7, and elsewhere in the specification. The corresponding stage of mammalian development is called a "blastocyst". A blastocyst is "the modified blastula of a placental mammal" (Merriam Webster's Collegiate Dictionary, tenth edition, Springfield Mass., 1993). It is clear from the specification that this is intended to be included in the invention.

The Examiner also states that the specification fails to teach inducing an organ *in vitro* for any mammalian species and thus fails to provide sufficient support for the full scope of the claimed invention. Applicants respectfully submit that mammalian organs can be induced *in vitro* using the same methods that are described in the specification for *Xenopus* and other species, without undue experimentation. The Examiner has not presented any evidence to cast doubt on applicants assertion to this effect.

The Examiner further argues that *ex vivo* organogenesis is scarce, if any, on *in vitro* induced organs in vertebrates other than amphibians. Applicants respectfully submit that the fact that reports of organogenesis may be scarce in vertebrates other than

amphibians is not relevant to the patentability of the present invention. The present methods are new, and the fact that previously described methods may have been more, or less, successful, should not reflect either favorably or unfavorably on the presently claimed method. Applicants have described specific examples of methods that should be successful in mammals as well as in the lower vertebrates, such as xenopus. The examiner has presented no convincing reason to doubt applicants' assertions in this regard.

The Examiner argues that the specification is silent with regard to how such a transplant could be done without disturbing the development of a fetus in a mammal, and that problems with allogenic rejection would preclude successful transplantation. Applicants respectfully disagree. It is first noted that the invention is not specifically directed to fetal transplants. Transplantation of allogenic tissues into children and adult humans has been carried out successfully, for example in the case of skin, kidney, liver, lung, heart and other organs. Tissue matching and/or the use of immunosuppressive drugs enables many of the recipients of these transplants and the transplanted organs to function well for extended and even indefinite periods of time. Furthermore, fetal surgery has been carried out on a fairly routine basis for a number of years. It is respectfully submitted that no more than routine experimentation is required to overcome the problems indicated by the Examiner. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 112, second paragraph

Claims 25-27 are newly rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. The Examiner appears to take the position that the recited method steps are not clearly related to the result obtained. This rejection is respectfully traversed.

The recited method steps clearly describe a means of obtaining an organ that functions *in vivo*: 1) determining the stage of the recipient vertebrate, 2) culturing an organ induced from ectoderm region which has been cut off from the blastula to the same stage, and 3) transplanting the cultured *in vitro* induced organ into the recipient. According to the invention, these steps will result in an organ that functions *in vivo* in the

recipient vertebrate. If this wording is still considered to be indefinite, the Examiner's suggestions for acceptable wording would be welcomed.

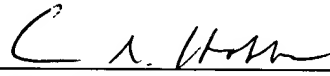
Rejection under 35 USC § 102(a)

Claims 25-27 are newly rejected under 35 USC § 102(a) as being anticipated by Ninomiya et al. for the reasons set forth on pages 10-11 of the Action. A translation of the originally filed Japanese priority application is submitted herewith. It can be seen by reviewing this document that priority to the claimed invention preceeds the publication date of the cited reference. Withdrawal of the rejection is respectfully requested.

In view of the above amendments are arguments, it is believed the application is in condition for allowance, and Notice to that effect is respectfully requested. If any minor issues remain in the application that might be resolved by a telephone discussion, the Examiner is invited to telephone the undersigned.

Please charge any additional fee deemed due to Deposit Account No. 22-0261 and advise us accordingly.

Respectfully submitted,



Ann S. Hobbs, Ph.D.

Reg. No. 36,830

VENABLE

Post Office Box 34385

Washington, DC 20043-9998

Telephone: (202) 344-4800

Direct dial: 202-344-4651

Telefax: (202) 344-8300